REMARKS

The office action has been studied carefully and the claims have been redrafted to overcome the objections noted. More particularly, the objections to the claims based on Section 112 have been cured by removing the objectionable language and reformulating the claims so that they are more precise and definite. All prior claims have been cancelled and new claims 38 to 49 are presented.

It is respectfully pointed out with regard to the objections concerning Section 112 with reference to the written disclosure, that the new claims have been formulated to comport with the specification, and what is now claimed was and is described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention of claims 38 to 49. The Examiner's comment regarding that the underlying detailed identification is missing of what exactly in the second constituent causes the inhibition of the activity, is not well founded. Applicant's duty is to point out with particularity and to distinctly claim the novelty and unobviousness of the invention. How it works or why it works, is of no consequence. The new claims recite with particularity and distinction what the second constituent is and what its concentration is. The specification supports the new claims by showing experiments that successfully achieve the desired result.

More particularly, the present application teaches, in Examples 3 and 5, respectively, the conditions for *in vitro* or *in vivo* inhibition of heparanase glycosidase catalytic activity. Specifically, Example 3 teaches that "active 50 kDa recombinant heparanase (10 ng/ml) was incubated with sulfate labeled ECM in the absence or presence of either lysed eosinophils, or, as a control, lysed human foreskin fibroblasts" (page 43, paragraph 189), and further along, the application teaches that "Complete inhibition of activity was obtained even at an heparanase concentration of 1 μg/ml, representing an estimated excess of MBP over heparanase of about 2.5 folds" (page 43, paragraph 189). Furthermore, the specification teaches that for the method of inhibiting

heparanase activity *in vivo*, incubating B-16 melanoma cells with 180μg/ml inhibited their tumorogenic capacity, which has been previously shown by the inventors to be directly correlated with heparanase activity. Thus, the man skilled in this art will be able, with the conditions described in the application, to understand, without undue experimentation, which conditions are suitable for carrying out the present invention.

Some of the new claims recite "the 117 amino acid residue MBP". Support for this recitation may be found on page 17, which refers to the amino acid content of the MBP protein, and recites that 14% of the residues are arginine, i.e., 17/117 amino acids, thus supporting that the MBP used in the present invention is the 117 amino acid residue MBP.

The new claims 38 to 49 are limited to eosinophil cell lysate and an eosinophil secondary granules basic protein, and mixtures thereof. The eosinophil secondary granules basic protein is recited in dependent claims to be selected from the group consisting of the 117 amino acid residue of MBP (Major Basic Protein), ECP (Eosinophil Cationic Protein), EPO (Eosinophil Peroxidase) and EDN (Eosinophil Derived Neurotoxin). However, the inventors have used proteins derived from cells (eosinophils), tissues (eosinophils are part of a tissue - blood) that endogenously express said protein, as well as lysates thereof. It may be extrapolated, without undue experimentation, that since it is feasible to use a cell expressing said proteins endogenously, it is also feasible to use a cell line expressing said protein.

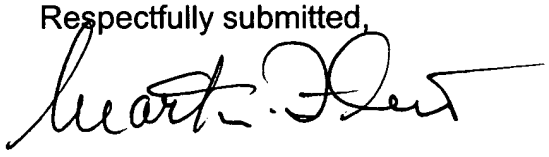
Claims 38 to 49 also include claims to a method for the inhibition of heparanase. The specification describes how MBP was able to inhibit the number of metastatic colonies in the lungs of mice injected with B16 melanoma cells. Moreover, the specification provides details as to the range of MBP sufficient to inhibit heparanase activity, being between 0.8-2x10^{-7}M (Example 3, page 49). Furthermore, mice treated with MBP were viable and, most importantly, showed no adverse or negative immune response (unpublished Inventor's data). Thus, the present invention is enabling for the claimed method.

With respect to the prior art cited and applied, namely, Davis et al describing interactions of eosinophil granule proteins with skin and Furuta et al describing eosinophil granule-derived major basic protein induced IL-8 expression in human intestinal myfibroblasts, neither reference is concerned with the problem concerning the present invention. Whatever compositions that may arguably be said to be disclosed, they do not meet the terms and limitations of the claims as now formulated. Neither reference suggests in any fashion the composition claimed or the use to which it is put for advantage.

In light of the foregoing remarks, this application should be in condition for allowance, and early passage of this case to issue is respectfully requested. If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

It is respectfully requested that, if necessary to effect a timely response, this paper be considered as a Petition for an Extension of Time, time sufficient, to effect a timely response, and shortages in this or other fees, be charged, or any overpayment in fees be credited, to the Deposit Account of the undersigned, Account No. 500601 (Docket No. 7640-X04-017).

Respectfully submitted,



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